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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,000	02/10/2006	Paul J. Coleman	21485YP	2668

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EXAMINER	
CHU, YONG LIANG	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,000	COLEMAN ET AL.	
	Examiner	Art Unit	
	Yong Chu	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☒ Claim(s) *1-6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 are pending in the instant application.

Information Disclosure Statement

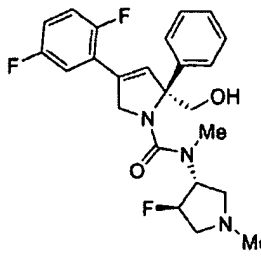
Applicants' Information Disclosure Statement, filed on 07/27/2006, has been considered. Please refer to Applicant's copies of the PTO-1449 submitted herewith.

Priority

This application is a 371 of PCT/US04/26242, filed on 08/11/2004, which claims benefit of U.S. Provisional Patent Application 60/495,466, filed on 08/15/2003.

Response to Lack of Unity/Restriction Requirement

Applicants' election without traverse of Group I, are drawn to products of formula



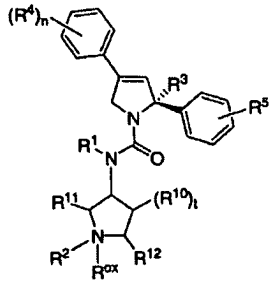
(I). Applicants further elected species of compound 2-6a on page 74 of the Specification for initial search purpose.

Status of the Claims

Claims 7-9 have been withdrawn by Applicants due to the restriction requirement.

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:

A compound of the Formula I  according to claim 1, wherein:

$\mathbf{R^1}$ and $\mathbf{R^2}$ are H, or $(C_1\text{-}C_6)$alkyl;

$\mathbf{R^3}$ is $C_1\text{-}C_{10}$ alkyl-O-$\mathbf{R^d}$, wherein $\mathbf{R^d}$ is H or $(C_1\text{-}C_6)$alkyl;

$\mathbf{R^4}$ is halo; $\mathbf{R^5}$ is hydrogen;

$\mathbf{R^{10}}$ is selected from F and CH_2F; $\mathbf{R^{11}}$ and $\mathbf{R^{12}}$ are independently selected from H and –CH_2F; and the remaining substituents are defined as in claim 1, a pharmaceutically acceptable salt or stereoisomer therefore, or a pharmaceutical composition comprising a compound of claim 1.

As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matter of claims 1-6 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups, which are chemically recognized to differ in structure, function, and reactivity. Therefore, claims 1-6 are under examination on the merits.

Claim Rejections - 35 USC § 103

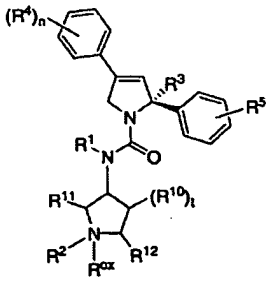
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 are rejected under 35 U.S.C. 103 (a) as unpatentable over Breslin et al., U.S. Patent No. 7,235,580 ("the `580 patent"), and in view Patani et al. *Chem. Rev.*, 1996, Vol. 96, pp.3147-3176 ("Patani et al").

Applicants' instant elected invention of claims 1-6 relates to a compound of the Formula I  according to claim 1, wherein:

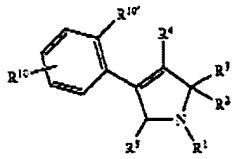
$\mathbf{R^1}$ and $\mathbf{R^2}$ are H, or $(C_1\text{-}C_6)$alkyl;

R^3 is C_1-C_{10} alkyl-O-R^d, wherein R^d is H or (C_1-C_6)alkyl;

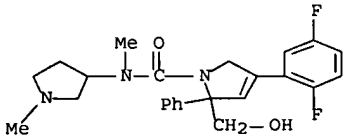
R^4 is halo; R^5 is hydrogen;

R^{10} is selected from F and CH_2F; R^{11} and R^{12} are independently selected from H and –CH_2F; and the remaining substituents are defined as in claim 1, a pharmaceutically acceptable salt or stereoisomer therefore, or a pharmaceutical composition comprising a compound of claim 1.

Determination of the scope and content of the prior art (MPEP §2141.01)



The `580 patent discloses a class of compounds of formula II

In addition, a specific compound (CAS RN 686320-55-8)  was disclosed, which is related to the instant claimed sub-genus, wherein:

R^1 and R^2 are (C_1-C_6)alkyl;

R^3 is C_1-C_{10} alkyl-O-R^d, wherein R^d is H;

R^4 is halo; R^5 is hydrogen;

R^{10} is H; R^{11} and R^{12} are H.

In addition, the prior art further suggests that the pyrrolidine ring as R^c can be further optionally substituted with R^{11}, wherein R^{11} as halo (i.e. item 5), which is -F, -Cl, or –Br, known to one ordinary skilled in the art. These compounds are used for

inhibiting the ATPase hydrolysis, and could be used for treating certain types of cancers.

Patani et al. taught fluorine vs hydrogen replacement as monovalent bioisosteres at page 3149, especially at table 4 of side-by-side comparision of –H vs. –F at the cyclo-ring system with IC_{50} testing data support.

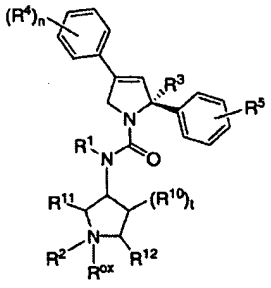
Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the `580 patent and the instantly claimed invention, is that the prior art teaches a specific compound with $\mathbf{R^{10}}$ as –H, but does not teach a compound with $\mathbf{R^{10}}$ as –F or $-CH_2F$, as claimed by the instant application.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

One skilled in the art would have found that the claimed compounds and compositions are *prima facie* obvious over the combined prior art teachings. It is because this difference of $\mathbf{R^{10}}$ as –H vs –F was taught and suggested by Patani et al. -F vs -H replacement as monovalent bioisosteres, and/or by the `580 patent, which suggests that the pyrrolidine ring as $\mathbf{R^c}$ can be further optionally substituted with $\mathbf{R^{11}}$, wherein $\mathbf{R^{11}}$ as halo (i.e. item 5). In addition, the prior arts and instant application all teach related art as pharmaceutical applications. Therefore, the instantly claimed invention is obviousness.

Claims 1-6 are rejected under 35 U.S.C. 103 (a) as unpatentable over Arrington et al., U.S. Patent Application No. 10/517,559 ("the `559 application"), and in view Patani et al. *Chem. Rev.*, 1996, Vol. 96, pp.3147-3176 ("Patani et al").

Applicants' instant elected invention of claims 1-6 relates to a compound of the Formula I  according to claim 1, wherein:

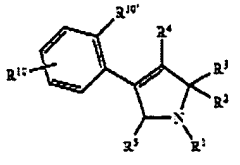
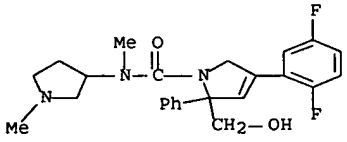
$\mathbf{R^1}$ and $\mathbf{R^2}$ are H, or $(C_1\text{-}C_6)$alkyl;

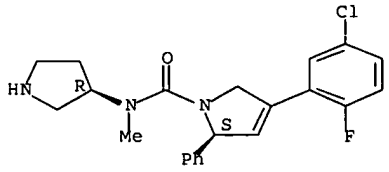
$\mathbf{R^3}$ is $C_1\text{-}C_{10}$ alkyl-O-$\mathbf{R^d}$, wherein $\mathbf{R^d}$ is H or $(C_1\text{-}C_6)$alkyl;

$\mathbf{R^4}$ is halo; $\mathbf{R^5}$ is hydrogen;

$\mathbf{R^{10}}$ is selected from F and CH_2F; $\mathbf{R^{11}}$ and $\mathbf{R^{12}}$ are independently selected from H and –CH_2F; and the remaining substituents are defined as in claim 1, a pharmaceutically acceptable salt or stereoisomer therefore, or a pharmaceutical composition comprising a compound of claim 1.

Determination of the scope and content of the prior art (MPEP §2141.01)

The `559 application discloses a class of compounds of  , with specific compound (CAS RN 686320-55-8)  and (CAS RN



639075-03-9) were disclosed, which are related to the instant claimed sub-genus, wherein:

R^1 and R^2 are H or (C_1-C_6)alkyl;

R^3 is C_1-C_{10} alkyl-O-R^d, wherein R^d is H;

R^4 is halo; R^5 is hydrogen;

R^{10} is H; R^{11} and R^{12} are H.

In addition, the prior art further suggests that the pyrrolidine ring as R^c can be further optionally substituted with halo, which is -F, -Cl, or –Br, known to one ordinary skilled in the art. These compounds are used for inhibiting the ATPase hydrolysis, and could be used for treating certain types of cancers.

Patani et al. taught fluorine vs hydrogen replacement as monovalent bioisosteres at page 3149, especially at table 4 of side-by-side comparision of –H vs. –F at the cyclo-ring system with IC_{50} testing data support.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the `559 application and the instantly claimed invention, is that the prior art teaches a specific compound with R^{10} as –H, but does not teach a compound with R^{10} as –F or $-CH_2F$, as claimed by the instant application.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

One skilled in the art would have found that the claimed compounds and compositions are *prima facie* obvious over the combined prior art teachings. It is

because this difference of R^{10} as –H vs –F was taught and suggested by Patani et al. -F vs -H replacement as monovalent bioisosteres, and/or by the `559 application, which suggests that the pyrrolidine ring as R^c can be further optionally substituted with halo. In addition, the prior arts and instant application all teach related art as pharmaceutical applications. Therefore, the instantly claimed invention is obviousness.

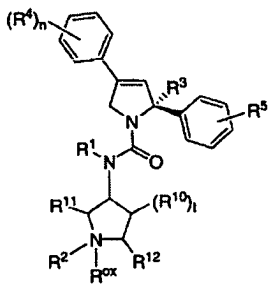
Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 9 of the `580 patent. Although the conflicting claims are not identical, they are not patentably distinct from each other because they teach the same claimed sub-genus.

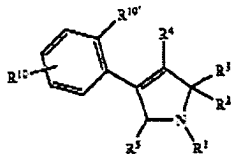


The instant application teaches a compound of the Formula I according to claim 1, wherein:

$\mathbf{R^1}$ and $\mathbf{R^2}$ are H, or $(C_1\text{-}C_6)$alkyl;

$\mathbf{R^3}$ is $C_1\text{-}C_{10}$ alkyl-O-$\mathbf{R^d}$, wherein $\mathbf{R^d}$ is H or $(C_1\text{-}C_6)$alkyl;

a pharmaceutically acceptable salt or stereoisomer therefore, or a pharmaceutical composition comprising a compound of claim 1.



The `580 patent discloses a class of compounds of formula II Although the conflicting claims are not identical, they are not patentably distinct from each other because they teach the same claimed sub-genus, wherein $\mathbf{R^3}$ as $C_1\text{-}C_{10}$ alkyl-O-$\mathbf{R^d}$, and $\mathbf{R^2}$ (in the prior art) as a phenyl. Therefore, claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting.

Claim Objections

Claims 1-6 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra.

Conclusion

- Claims 1-6 are rejected.
- Claims 1-6 are objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yong Chu, Ph.D.
Patent Examiner
Art Unit 1626

REBECCA ANDERSON
PRIMARY EXAMINER

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